REMARKS

Applicants have canceled claim 1, necessitating change of dependency of claims 3-5, 10-11, 13, 15-17. Further, Applicants have amended claim 2 and added new claim 39 to particularly point out and distinctively claim the subject matter that Applicants regard as their invention. Support for the amendment to claim 2 can be found in the specification, e.g., at page 3, lines 4-12. Support for new claim 39 can be found in Table 3 at page 21. No new matter has been introduced.

After amendments, claims 2-6, 10, 11, 13, 15, 16 and 39 will be under examination. Reconsideration of this application is respectfully requested in view of the following remarks:

Rejections under 35 U.S.C. 102

The Examiner maintained the rejection of claims 1-5, 11-13 and 15-16 as anticipated by Yamaoka et al.("Yamaoka") [1]. See the Office Action, item 8, at pages 7-8.

With cancellation of claim 1, claim 2 is now the only independent claim. Claim 2, as amended, covers an immunomodulator having an APC-targeting molecule ***coupled with an antigen***. The APC-targeting molecule includes a Class II MHC binding site and a T-cell receptor binding site of a superantigen. Further, the T-cell receptor binding site has one or more mutations, resulting in reduced T-cell proliferation activity compared to the wild type T cell receptor binding site.

Yamaoka discloses that the mutants of superantigen Streptococcal pyrogenic exotoxin C (SEP-C) have reduced T-cell activation activity. These mutated SEPC superantigens "were generated by site-directed mutagenesis as GST fusion proteins and purified by GST-Sepharose 4B, and ***GST was cleaved***." See page 5022, left column.

Nothing in Yamaoka suggests using a mutated superantigen ***coupled with an antigen*** as an immunomodulator. In the reference, the fusion proteins of GST/SEP-C mutants disclosed in Yamaoka were for the sole purpose of facilitating purification of the SEP-C mutants; indeed, GST was cleaved before the immune modulation activity of the SEP-C mutants were tested. See

[1] Please note that the Examiner has included claim 12 inadvertently, as this claim was previously cancelled.

e.g., page 5022, left column. In other words, Yamaoka discloses that SEP-C mutants, ***without fusing with an antigen***, alter immune responses compared to the wild type SEP-C. By contrast, the immunomodulator of claim 2 has an APC-targeting molecule ***coupled with an antigen***. Therefore, Yamaoka does not anticipate claim 2. By the same token, claims 3-5, 11, 13 and 15-16, all depending from claim 2, are also not anticipated by Yamaoka.

Rejections under 35 U.S.C. 112, first paragraph (written description)

The Examiner acknowledged that Applicants have disclosed adequately the APC-targeting molecules that ***mimic*** a superantigen in the original application in view of our previous response filed Feb. 13, 2006. See the Office Action, page 6, third paragraph. However, she maintained the rejection of claims 1-6, 11, 13, and 15-16 on the ground that there is no adequate written description to show Applicants' possession at the filing date APC-targeting molecules that are ***structurally*** a superantigen. See the Office Action, item 7, pages 5-7.

In response, Applicants have deleted the term "structurally a superantigen" from claim 2, the only claim that recites this term. Further, Applicants have specified in claim 2 that the recited APC-targeting molecule includes a Class II MHC binding site and a mutated T-cell receptor binding site of a superantigen, that the mutated T-cell receptor binding site has reduced T-cell proliferation activity compared to its wild type counterpart.

It is well known in the art that a superantigen contains two structural and functional domains: the MHC Class II binding domain and the T-cell receptor binding domain. See Proft et al. J. Exp. Med. 1999, 89-101; and Li et al. Annu. Rev. Immunol. 1999, 435-66, copies of which are attached hereto as Exhibits A and B. The specification identifies amino acid residues that are important to T-cell receptor binding. See, e.g., page 14, lines 7-9. It also provides examples of APC-targeting molecules having mutated T-cell receptor binding sites of a superantigen. See, e.g., Example 2 at pages 10-15. It further shows that these mutants have reduced T-cell proliferation activity. See, e.g., Example 6 at pages 20-21. Given this specific teaching and common knowledge of superantigen, one with ordinary skill in the pertinent art would

understand that Applicants were in possession of the immunomodulator of claim 2 at the time the application was filed.

For the reasons set forth above, Applicants submit that this rejection for inadequate written description has been overcome

Rejections under 35 U.S.C. 112, first paragraph (enablement)

The Examiner further rejected claims 1-6, 10-11, 13 and 15-16 for failing to comply with the enablement requirement, a new ground of rejection. According to the Examiner, the specification does not teach one of ordinary skill in the pertinent art how to make and use an immunomodulator containing "a part of a superantigen" or a molecule which is "structurally a superantigen." See the Office Action, item 10, pages 8-10.

Applicants have canceled claim 1, which recites "a part of a superantigen," and removed "structurally a superantigen" from claim 2. These amendments have rendered the grounds for rejection moot.

As stated above, it is well known in the art that a superantigen contains one Class II MHC binding site and one T-cell receptor binding site. The specification also teaches how to identify amino acid residues important to T-cell receptor binding, how to mutate these relevant amino acid residues, and how to determine whether the mutations reduce the T-cell proliferation activity of the APC-targeting molecule as recited in claim 2. See, e.g., page 14, lines 7-9; Example 3, at pages 16-18. Taken together, the specification clearly teaches an ordinarily skilled person how to make and use the claimed invention.

In view of the above remarks, Applicant respectfully request withdrawal of the rejection for lack of enablement.

Rejections under 35 U.S.C. 112, second paragraph

The Examiner also rejected claims 1-6, 10-11, 13, and 15-16 as being indefinite on three grounds. See the Office Action, item 6, pages 3-5. Applicants respectfully traverse each of the grounds below:

First, the Examiner pointed out that the terms "immunomodulator" and "immunomodulatory" are indefinite as to the direction and the degree of modulation. Applicants have deleted the term "immunomodulatory" from claims 2, 10-11, and 13. Applicants, however, disagree with the Examiner that the term "immunomodulator" is indefinite. Immunomodulator is a well-defined term in the pertinent art. For example, Merriam-Webster's Medical Dictionary defines "immunomodulator" as *a chemical agent that modifies the immune response or the functioning of the immune system.* See Exhibit C. Further, according to On-line Medical Dictionary, an immunomodulator is *a drug such as interleukin-2 that alters, suppresses or strengthens the body's immune system.* See Exhibit D. It appears that the Examiner has misread the application, judging from the statement that "it is unclear how the invention can be both simultaneously capable of enhancing and suppressing (i.e. modulating) an immune response, since these are mutually exclusive possibilities." See the Office Action, page 4, fifth paragraph. An immunomodulator either enhances ***or*** suppresses an immune response. It does not enhance ***and*** suppress an immune response at the same time.

Second, according to the Examiner, the terms "fully functional" and "little or no activity" are relative terms, which render the claims indefinite. Applicants have deleted the terms "fully functional" and "little or no ability" from claims reciting either one. Further, Applicants have amended claim 2 to specify that the APC-targeting molecule includes a mutated T-cell receptor binding site, resulting in reduced T-cell proliferation activity when compared to its wild type counterpart.

Third, the Examiner stated that the term "non-immunogenic" recited in claim 13 contradicted the term "immunomodulatory" recited in the same claim. Applicants have deleted the term "immunomodulatory" from claim 13.

For the above stated reasons, Applicants submit that grounds for the indefiniteness rejection have been successfully traversed.

CONCLUSION

Applicant submits that the amendments to pending claims have overcome all grounds for rejections/objections asserted by the Examiner. Claims, as pending, define subject matter that is definite, sufficiently described, enabled and novel. Therefore, Applicant respectfully request that all rejections/objections be withdrawn and the pending claims be allowed.

Enclosed is a $60 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 8/24/06

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